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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,907	05/24/2000	RAINER HOFFMANN		3754

7590 10/22/2004

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 10/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/508,907	HOFFMANN ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-75 and 78-87* is/are pending in the application.

4a) Of the above claim(s) *86 and 87* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-75 and 78-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/04/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicant's amendment, filed 08/09/2004.

Claims 31-87 have been added, and claims1-30, 76 and 77 have been canceled.

Claims 86 and 87 are withdrawn from consideration as being directed to new invention of a method of making a product that was not originally presented.

Claims 31-75, and 78-85 are included in the prosecution.

The following rejections has been discussed in the previous office action, and are repeated for reasons of record:

Applicants have not responded to the rejection made to the specification by amendment or argument, thus, the rejection is repeated.

Specification

1. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in

upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.
(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

2. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. Example of typographical errors is on page 10, last line the word "ethylene glycol " is misspelled.

The following new ground of rejections are necessitated by applicants' amendment:

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 31-75, 78-85 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the morphine, does not reasonably provide enablement for all morphine alkaloids such as: codeine, heroin, ethylmorphine, levorphanol, or hydromorphone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the breadth of the claims; the state of the prior art; the relative skill of those in the art; the amount of direction or guidance presented; the predictability or unpredictability of the art; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The nature of the invention:

The invention provides transdermal or transmucosal composition consisting essentially of a morphine acid addition salt with an organic acid, and one of solvent or suspending medium. The entire specification disclosed morphine, and not the whole class of morphine alkaloids. Support for species does not support the genus.

The breadth of the claims: The claims are very broad. The claims encompass a wide class of morphine alkaloids with many different species of organic acid including codeine, heroin, ethylmorphine, levorphanol, and hydromorphone, and further different combinations with solvent or suspending agent.

The state of the prior art:

The state of the art recognized transdermal composition comprising morphine acid addition salt with organic acid and one of DMSO, ethylene glycol, or oleic acid, see US 4,626,539, US 879,297, and EP 0 321 870. However, the art does not teach the morphine acid addition salt with organic acid and olive oil.

The relative skill of those in the art:

The relative skill of those in the art is high.

The amount of direction or guidance presented:

The specification provides no guidance, in the way written description, on each species of morphine alkaloids including codeine, heroin, ethylmorphine, levorphanol, or hydromorphone as acid addition salt with each of the claimed organic acid and each of the solvent or suspending agents. The specification disclosed only morphine acid addition salt with organic acid and olive oil as demonstrated by figure 4. It is not obvious from the disclosure of morphine if the acid addition salts of other morphine alkaloids will

work with other solvents or suspending agents other than olive oil and provide the same flux. In re *Dreshfield,* 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in detail. A disclosure should contain representative examples which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See *In re Riat et al.* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr et al.* (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

The predictability or unpredictability of the art:

The lack of guidance from the specification and from the prior art with regard of a transdermal or transmucosal composition consisting essentially of a morphine as an addition salt with an organic acid and solvent makes practicing the claimed invention unpredictable in the terms acid addition salts of other species of morphine alkaloids in combination with different solvents or suspending agents.

The presence or absence of working examples:

The specification discloses only morphine in all the examples. No working examples to show the use of other species of morphine alkaloids. Therefore, the specification has

enabled only the species "morphine". Also the specification enabled acid addition salt of morphine and olive oil, figure 4.

The quantity of experimentation necessary:

Since the behavior of other species of morphine alkaloids, other than morphine, is unpredictable, and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue experimentation to determine the flux of all the species of the morphine alkaloids with olive oil.

5. Claims 31-75, and 78-85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification provides no support for transdermal or transmucosal composition for administering more than one morphine alkaloid, and in particular "morphine". The support in the specification in figure 4 and the examples is for one morphine salt and olive oil, not more than one salt. No support for the claimed genus "morphine alkaloids" with other suspending agents or solvents. Support for a species does not support the genus.

Claim 74 recites "plurality of morphine alkaloids" that lacks support in the specification.

Furthermore, the amendment to claim 31 to recite the bond between C_7/C_8 "is alternatively saturated" introduces new subject matter that lacks support in the specification.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 31-75, 78-85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 lacks clarity as the claim recites "composition for administering at least one morphine alkaloid" and later in the claim, the claim recites "the composition consisting essentially of a morphine acid addition salt", and again the claim broadens the scope by reciting that the "a morphine acid addition salt" is formed by the reaction of "at least one morphine alkaloid" that encompasses alkaloids other than morphine. Clarification is requested.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "bond C_7/C_8 is alternatively saturated" in claim 31 is used by the

claim to mean "no double bond between C_7/C_8", while the formula shows unsaturated bond between C_7/C_8. Clarification is requested.

Claim 32 fails to further limit the subject matter of a previous claim 31 that has a closed language "consisting essentially of a morphine acid addition salt". Claim 32 broadens the scope of claim 31.

Claims 33-40, 42-44, 48, 50, 51, 55, 57, 59, 61-68, 70, 71 recite the limitations "(B)(1), (B)(2), (B)(3), (B)(4), (B)(5), (B)(6), (B)(7)" in claim 31. There is insufficient antecedent basis for this limitation in claim 31.

Claim 43 recites the limitation "polysubstitution" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 74 fails to further limit claim 31, and broadens the scope of claim 31 by reciting "polarity of morphine alkaloid". Claim 31 includes the closed language "consisting essentially of a morphine".

Claim 75 fails to further limit the scope of claim 31, and broadens its scope because claim 31 recites the organic acid is selected from group consisting of specific acids, and claim 75 broadens the scope to the generic broad term "organic acid".

Claims 78 and 79 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 31 limits the composition to be "consisting essentially of a morphine, an organic acid, and solvent

or suspending agent", while claims 78 and 79 further adding ingredients to the composition.

Regarding claim 81, the phrase "as a TTS" renders the claim indefinite because it is unclear whether the TTS is the only form or an example of the form.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 31-75, 78-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US 4,626,539 ('539), US 4,879,297 ('297) or EP 0 321 870 ('870).

US '539 teaches opioid-containing pharmaceutical composition which as useful in effecting transdermal delivery of therapeutic doses of opioid to systemic circulation of mammal. The references disclosed composition comprising acidic salts of morphine such as sulfonates, and one of polyethylene glycol and oleic acid. The composition can be in the form of cream, lotion or patch (abstract, col.1, lines 60-65; col.2, lines 18-34; col.3, lines 37-38; col.4, lines 2-23).

US '297 teaches opioid-containing pharmaceutical composition which as useful in effecting transdermal delivery of therapeutic doses of opioid to systemic circulation of mammal. The references disclosed composition comprising acidic salts of morphine such as sulfonates, and one of polyethylene glycol and oleic acid. The composition can be in the form of cream, lotion or patch (abstract, col.1, lines 22-64; col.3, lines 3-17; col.4, lines 62-63).

EP '870 teaches skin preparation comprising opioid such as morphine as acid addition salts with organic acid such as benzoic acid and solvent such as DMSO, or glycerol (abstract; page4, lines 32-35; page 5, lines 37-39; page 6, lines 3-12).

Therefore, the art recognized the transdermal or transmucosal composition comprising morphine salt with an organic acid and a solvent. However the references do not teach the specific organic acid. The specific organic acids claimed by applicants do not impart patentability to the claims, absent evidence to the contrary.

Accordingly, it would have been obvious to one having ordinary skill in the ad at the time of the invention to produce transdermal or transmucosal composition comprising acid addition salt of morphine with the an organic acid as disclosed by any

of the references, and select the organic acid according to the specific formulation, with reasonable expectation of having pain relief transdermal or transmucosal formulation with enhanced activity.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

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